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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,441	12/20/2001	Stephen Quirk	1443.024US1	2667
21186	7590	05/17/2005	EXAMINER	
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.			KISHORE, GOLLAMUDI S	
P.O. BOX 2938			ART UNIT	
MINNEAPOLIS, MN 55402-0938			PAPER NUMBER	
			1615	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,441	QUIRK, STEPHEN	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 16-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2-28-05</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The RCE dated 2-28-05 is acknowledged.

Claims included in the prosecution are 1-15. Claims 16-27 remain withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 6 and 11 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for disulfide cross-linkers, does not reasonably provide enablement for generic 'cross-linker that can form a pore upon exposure to a reducing agent". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant has not adequately described in the specification what cross-linkers other than those containing disulfide bridges can be used in practicing the invention. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to disulfide cross-linking agents disclosed as having the intended function.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steiner (4,925,673) in combination Mathiowitz (5,271,961) and Margolin (6,541,606).

Steiner discloses protenoid delivery systems of thermally condensed amino acids (abstract and examples). What is lacking in Steiner is the teaching of further cross-linking using disulfide bridges.

Mathiowitz while disclosing protein microspheres teaches that the microspheres can be modified for a given application chemically to produce a protein having enhanced or altered thermal stability, surface reactivity and others; one such modification suggested by Mathiowitz is cross-linking of the protein using agents such as glutaraldehyde (abstract, col. 5, lines 50-57; col. 6, lines 54-62). Mathiowitz however, does not teach disulfide cross-linking agents.

Margolin while disclosing stabilized protein formulations teaches cross-linking of the proteins using several chemical agents including aldehydes and thio-labile linkers having the structure R'-S-S-R. According to Margolin, thio-labile cross-linkers are reversible cross-linkers and several disulfide cross-linkers are known and commercially available. (Abstract, col. 24, line 29 through col. 26, line 61).

It would have been obvious to further modify the protenoids of Steiner introducing dithio linkages since Mathiowitz teaches that the protein microspheres can be modified

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for a given application and cross-linked using aldehydes such as glutaraldehyde and Margolin teaches that the equivalency between aldehyde cross-linking and thio-labile cross-linking. One of ordinary skill in the art would be further motivated to use thio linkage in view of Margolin's teachings of reversibility of thio linkages.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that the examiner assumed the equivalency between proteins and proteinoids. According to applicant, it is like comparing apples and oranges. The examiner disagrees since it is a comparison between apples since proteinoids are thermal protein polymers containing amino acids and proteins are polymers of amino acids (5,679,377, see col. 1, lines 25-50). Applicant's own statements on page 2 of the specification indicate that proteinoids are artificial amino acid polymers. Applicant argues that Steiner's disclosure teaches away from cross-linking since key feature in Steiner according to applicant is their ability to dissolve in near neutral blood and thereby release pharmacological agents in a desired physiological location. It is unclear to the examiner how this is teaching away since blood provides a reducing atmosphere (5,399,331 is cited of interest in this context, see col. 4, lines 33-35) for the reduction of the cross-linked disulfide bridges suggested by the secondary references. It is therefore, the examiner's position that cross-linking of the proteinoids of Steiner by disulfide bridges would not inhibit the release of the active agent. Applicant's arguments that cross-linking of proteins frequently results in insoluble products. The examiner agrees that cross-linking by irreversible cross-linking agents might lead to

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insoluble products. Hence the motivation for one skilled in the art to use cross-linking by disulfhydryde bridges since it is reversible.

5. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steiner (4,925,673) in combination Mathiowitz (5,271,961) and Margolin (6,541,606) as set forth above, further in view of McKenzie (JBC, vol. 275, No. 14, pp. 9970-9977, 2000) of record.

The teachings of Steiner, Mathiowitz and Margolin have been discussed above.

McKenzie while disclosing a new class of reductively activated peptide gene delivery agents teaches that peptides containing cysteine residues can be reversibly cross-linked with DNA and when this complex is administered, the reducing environment of the cell allows the disulfide cross-linked DNA condensates to undergo reduction and release DNA more readily than glutaraldehyde cross-linked DNA condensates. McKenzie also shows enhanced gene expression using this cross-linking method. (Page 9970, Fig. 1, Table 1, page 9976-9977.


One of ordinary skill in the art would be motivated further to use the reversible disulfide cross-linking for the protenoid delivery system of Steiner since McKenzie teaches enhancement of transcription activity using reversibly disulfide cross linking method.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK